

NATIONAL CENTRE FOR STREPTOCOCCUS

ANNUAL REPORT FOR APRIL 1, 2003 TO MARCH 31, 2004

Introduction

The National Centre for Streptococcus (NCS) continues to provide testing required to support national and provincial public health *Streptococcus* surveillance programs.

Current surveillance data is available on-line through our website at www.provlab.ab.ca. Quarterly and annual reports may be accessed as well as our Guide to Services and expected turn around times. A current summary of publications from the National Centre for Streptococcus is also available.

Goals and Objectives for the Past Year

Much of the work that was planned for 2003-04 was deferred while we negotiated additional national funding to support these efforts. Unfortunately, until additional funding is secured we are unable to initiate most of these projects.

1. Distribution of quarterly reports by hard copy to Provincial Public Health Lab Directors was discontinued as planned. These reports are available on-line through our website at www.provlab.ab.ca. We assume that this change has been acceptable to our customers since we have received no requests to receive these reports by hard copy.
2. Additional molecular investigation of an unusual phenotype of macrolide-resistant *S. pneumoniae* was deferred pending additional funding.
3. Investigate the national distribution and the molecular characterization of an erythromycin-resistant *S. pneumoniae* type 12F clone was deferred pending additional funding.
4. The implementation of rigorous clinical criteria for pneumococcal EIA resulted in the approval of very few requests for this assay. Only 9 of 25 samples received were approved for testing. Due to the infrequency of test requests, we did not implement the use of a clinical information form for this purpose.
5. Progress has been made with respect to the epidemiological investigation of *S. pneumoniae* infections through the *S. pneumoniae* Alberta Team (SPAT) that was created last year. Work is ongoing to secure funding for this initiative through Federal funding agencies (CIHR) and industrial (Wyeth) sources. Unfortunately, due to circumstances beyond the control of the NCS, the provinces of Saskatchewan and Manitoba are not part of this group as was originally planned. It is hoped that future projects can be expanded to include these two provinces.
6. The use of 16S rRNA sequencing to supplement the biochemical identification of atypical catalase-negative gram positive cocci was implemented specifically for isolates that are not easily identified by traditional biochemical testing. This tool has been useful in some situations, but we are still developing our testing and reporting algorithms in order to optimize its use.
7. None of the activities that were listed in the 2002-03 annual report as 'contingent on funding availability' were initiated. It is hoped that funding of this work will be secured in the coming year.

Activities

a. Reference Services

After steadily increasing numbers of specimens received at the NCS between 1991 and 2000, our test load has decreased slightly over the past three years. One reason for the decrease over the past year was the implementation of specific clinical criteria for Pneumococcal EIA testing in January, 2003. This resulted in a reduction of over 90% of the requests for this test. A reduced number of requests for group A serotyping may reflect decreasing invasive disease, since those agencies routinely submitting isolates to the NCS has not changed. As expected, on-going surveillance of invasive *Streptococcus* disease in Canada combined with newly implemented vaccine programs targeted at prevention of invasive pneumococcal disease in young children has resulted in a slight increase in the utilization of pneumococcal serotyping services offered by the NCS. Comparison of specimen numbers for the past four years is presented in Table 1. As in the past, the majority of the externally funded research projects processed by the NCS continues to be focused on pneumococcus surveillance. Services provided for research projects for 2003/2004 and the proportion of the total testing dedicated to this function are also identified in Table 1. Only externally funded research projects are listed.

Table 1. Specimen Volume and Research Testing

Total Test Requests	2000/01	2001/02	2002/03	2003/04	2003/04 Research	
					# Specimens	% Testing
Group A Serotyping	1111	1103	1133	973	5	0.5%
Group B Serotyping	425	209	279	205	58	28.3%
Pneumococcal Serotyping	1916	1980	1760	2074	927	44.7%
Identification	238	226	224	183	0	0
Pneumococcal Serology	256	351	301	25	0	0
Other	3	11	3	4	0	0
Total Isolates Received	3949	3880	3700	3464	990	28.6%

b. Laboratory Surveillance

All of the data presented in this section reflect passive surveillance only. The majority of all isolates tested at the NCS are recovered from normally sterile sites, and/or are associated with invasive disease. Occasionally noninvasive isolates are submitted due to atypical characteristics. Wherever possible, only one isolate was counted per patient, however specimen coding may have prevented interpretation of this information for some isolates.

All data from externally funded studies have been excluded from this report.

Group A Streptococcus

Historically the majority of the GAS that were submitted to the NCS for serotyping have come from Alberta, Ontario and Quebec (Figure 1). Over the past three years we have observed a substantial increase in GAS submitted from British Columbia. We believe that this increase represents enhanced surveillance, and may not necessarily reflect an increase in the incidence of invasive GAS disease in that province. GAS isolates submitted from these four provinces account for 92% (990 of 973) of the 2003/04 GAS collection.

Figure 1.

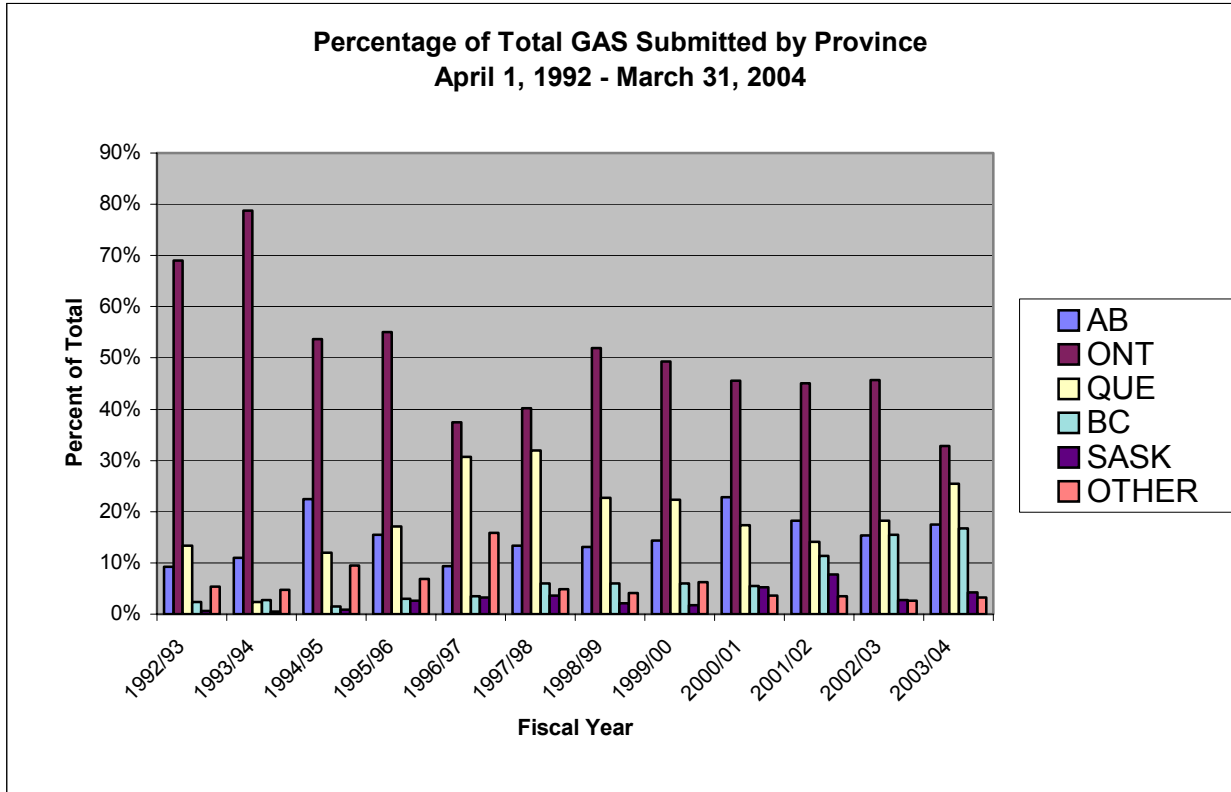


Table 2 presents M type distribution for the past year and comparative data for 2002/03 and 2001/02. Specific M types are known to be poorly antigenic, making it difficult to prepare the M antisera necessary for serological M type classification. Serotypes M28 and M77 fall into this category. These serotypes are more easily classified according to the AOF type, using antisera specific for the serum opacity factor produced by OF positive strains. The AOF type is, with few exceptions, consistent with the M type, and strains typed as 28 or 77 by either method have been listed together in this report.

Table 2. Group A Streptococcus M type Distribution

M type	2003/04			2002/03			2001/02		
	# Cases	Rank	% of total	# Cases	Rank	% of total	# Cases	Rank	% of total
M1	277	1	30.9	295	1	29.7	186	1	19.0
AOF [†] 28	100	2	11.1	68	3	6.8	56	6	5.7
M12	65	3	7.3	89	2	9.0	79	3	8.1
M4	46	4	5.1	44	4	4.4	64	4	6.5
M/AOF [†] 77	33	5-6	3.7	43	5	4.3	40	7	4.1
M91	33	5-6	3.7	19	14-16	1.9	18	15	1.8
M82	32	7	3.6	28	10-11	2.8	15	16	1.5
M89	28	8	3.1	29	8-9	2.9	35	8/9	3.6
M5	25	9-10	2.8	28	10-11	2.8	62	5	6.3
PT2967	25	9-10	2.8	27	12	2.7	35	8/9	3.6
M11	23	11	2.6	38	7	3.8	20	13	2.1
M2	20	12	2.2	18	17	1.8	22	12	2.3
M83	18	13	2.0	20	13	2.0	11	18	1.1
M3	17	14	1.9	39	6	3.9	104	2	10.6
M nt*	47		5.2	58		5.8	80		8.2
Other	108		12.0	151		15.2	151		15.4
Total	897			994		100	978		100

NA = not available

[†]AOF = Anti Opacity Factor type

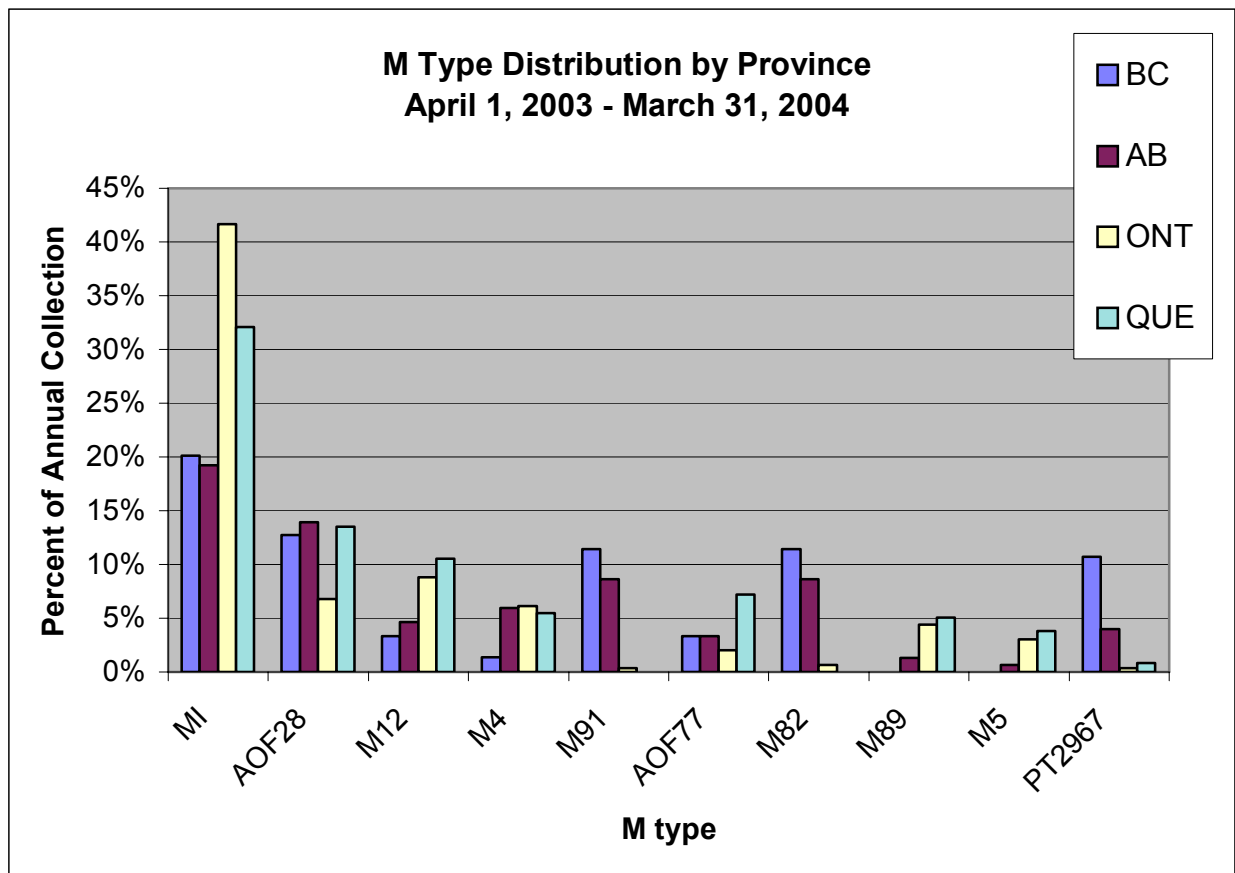
*nt = not typable

With the exception of 2000/01 when M1 fell to second place, this M type has consistently been the most frequently encountered serotype since the NCS began reporting national GAS seroprevalence in 1992. M1, AOF28, M12, M4 and M/AOF77 have been among the top 7 M types for the past three years. M91 was encountered twice as frequently in 2003/04 than in the previous two years (3.7% versus 1.9 and 1.8%).

The Provincial distribution of the top 10 ranking M types in the 2003/2004 collection, are presented in Figure 2. While M1 is frequently encountered in all regions, the predominance of this serotype in Ontario and Quebec is a continuation of a trend that was evident in 2002/03. In Ontario, this serotype accounted for 42% of the isolates, an increase from 32% in 2002/03. The prevalence in Quebec was similar for both years (38% in 2002/03 and 32% in 2003/04). In British Columbia, the prevalence of M1 has decreased from 34% in 2002/03 to 20% in 2003/04.

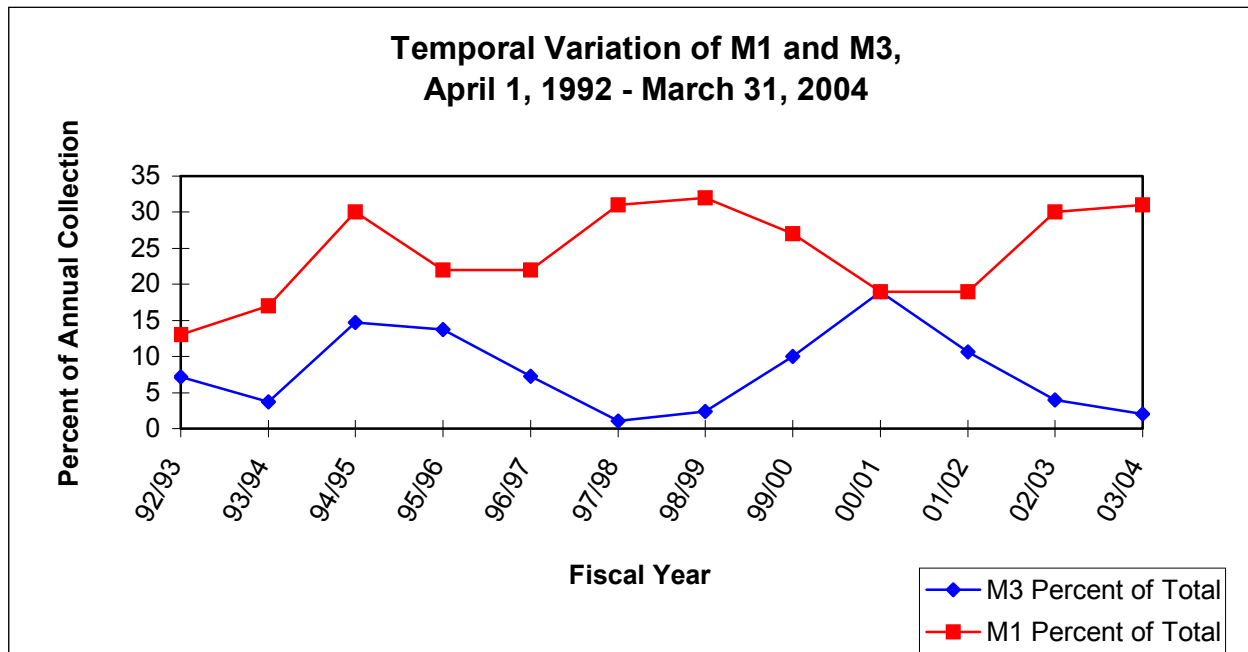
There is obvious geographic variation across Canada for some of the other M types. M5, M12 and M89 are more commonly encountered in the East, while M82, M91 and MPT2967 are predominant in the Western regions. AOF28 is common across Canada.

Figure 2.



The temporal variation of M1 over the past 12 years is compared with that of M3 in Figure 3. For the first four years of our surveillance, the ratio of these two types was relatively proportionate but in 1996/97, the prevalence of M3 began to decline followed by an increase in the prevalence of M1. During 2000/01 M3 was equally as important as M1 as a cause of invasive disease in Canada. The decline in M3 accompanied by an upswing in M1 observed over the past three years demonstrates an interesting evolving pattern in seroprevalence variation for these M types.

Figure 3.



GAS and Antibiotic Resistance

Antibiotic susceptibility of all GAS submitted for serotyping was determined by the disk diffusion method. Penicillin, erythromycin, clindamycin, chloramphenicol and vancomycin were routinely tested. Only data from Provinces submitting >50 isolates over the past year were analyzed in Table 3. Resistance to erythromycin was associated with MPT2967, M58 and M4.

Table 3. Proportion (%) of Antibiotic Resistance by Region for Group A Streptococci;
April 1/03 – March 31/04 (comparative data for April 1/02 - March 31/03)

Antibiotic	BC	AB	ON	QB	Other	Total
Erythromycin	16.8 (14.4)	8.0 (9.1)	7.8 (9.2)	9.7(11.7)	7.7 (17.0)	9.8 (10.9)
Clindamycin	2.0 (3.3)	0.7 (0)	1.0 (1.1)	3.0 (3.6)	0 (3.8)	1.6 (1.9)
Chloramphenicol	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Penicillin	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Vancomycin	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total # isolates tested	149 (153)	151 (154)	295 (437)	237 (197)	65 (53)	897 (994)

All erythromycin-resistant isolates were also screened for inducible resistance to clindamycin using the double disk test. Inducible resistance was detected in 55 of 88 (62.5%) of the erythromycin-resistant isolates.

Group B Streptococcus

The data presented in table 4 represents the number of cases of invasive disease for which isolates were submitted to the NCS for serotyping. These were primarily from the province of Alberta. Isolates from 114 of 137 cases received from April 1, 2003 – March 31, 2004, and 146 of 185 cases received from April 1, 2002 to March 31, 2003 were from that province. The data therefore may not be representative of national trends. Only one isolate per case was included in the analysis.

Table 4. Group B Streptococcus Serotype Distribution by Age for April 1, 2003 - March 31, 2004
(Comparative data for April 1, 2002 - March 31, 2003)

Serotype	<3 mon	3 mon-20 yr	21-50 yr	>50 yrs	Age not specified	Total
V & V / R	2(5)	0(0)	13(19)	24(26)	0(0)	39(50)
III & III / R	9(10)	1(3)	4(8)	12(15)	0(1)	26(37)
Ia & Ia / c	4(7)	0(1)	8(7)	12(19)	0(0)	24(34)
II & II / c	2(1)	0(2)	3(9)	9(12)	0(0)	14(24)
Ib & Ib/ c	2(1)	1(1)	2(3)	9(14)	0(0)	14(19)
IV	0(0)	0(0)	1(0)	2(1)	0(0)	3(1)
VI	0(0)	0(0)	0(1)	1(0)	0(0)	1(1)
VII	0(0)	0(0)	0(0)	0(1)	0(0)	0(1)
Not typable*	0(0)	0(0)	5(6)	11(12)	0(0)	16(18)
TOTAL	19(24)	2(7)	36(53)	80(100)	0(1)	137(185)

*Not typable = carbohydrate antigen not detected

Types V, III and Ia (with and without the c or R protein antigens) account for 65% of the disease represented by this sample. Isolates belonging to serotypes V, Ia, Ib, and II were associated with adult disease; 80 of 91 isolates (88%) belonging to these serotypes were recovered from patients ≥ 21 years of age. Nontypable isolates are most frequently encountered in older adults. Nine of 19 isolates (47%) that caused invasive disease in the youngest age group (<3 months) belonged to serotype III and III/R.

Five isolates from cerebrospinal fluid were submitted. Four of these were from children <3 months old; two belong to serotype III/R, one to serotype Ib/c and one to serotype II/c. The fifth CSF isolate was cultured from a 31 year old adult and belonged to serotype III.

GBS and Antibiotic Resistance

Antibiotic susceptibility of all GBS submitted for serotyping was determined by the disk diffusion method. Penicillin, erythromycin, clindamycin, chloramphenicol and vancomycin were routinely tested. Because the majority of the isolates were submitted from Alberta, data are presented for that province separately from the rest of Canada (TROC) in Table 5.

Overall, the proportion of erythromycin resistance is higher than that observed in 2002/03 with one quarter of all isolates showing resistance to this antibiotic. Elevated rates are also apparent for the rest of Canada. The proportion of clindamycin resistance has decreased in Alberta, but has increased for isolates submitted from other provinces. Readers are reminded that resistance rates for TROC should be interpreted with caution due to the small sample size. There is no obvious association between serotype and resistance to either of these antibiotics; resistance was encountered in all of the most common serotypes and in nontypable isolates.

Table 5. Proportion (%) of Antibiotic Resistance by Region for Group B Streptococci; April 1/03 – March 31/04 (comparative data for April 1/02 - March 31/03)

Antibiotic	Alberta	TROC	Total
Erythromycin	25.4 (21.2)	17.4 (12.8)	24.1 (19.5)
Clindamycin	9.7 (15.1)	8.7 (2.6)	9.5 (12.4)
Chloramphenicol	0(0)	0(0)	0(0)
Penicillin	0(0)	0(0)	0(0)
Vancomycin	0(0)	0(0)	0(0)
Total # isolates tested	114 (146)	23 (39)	1370 (185)

Streptococcus pneumoniae

The following analyses for April 1, 2000 to March 31, 2004 exclude data from isolates received from Laboratoire de Santé Publique du Québec (LSPQ), where serotyping for their provincial pneumococcal surveillance program is performed. Only isolates of less common serotypes are submitted to the National Centre for Streptococcus for factoring; data from these uncommon serotypes have been excluded in an effort to eliminate the resulting bias. Data specific for Quebec may be obtained by contacting the LSPQ directly. Please note that comparative data from previous years do not exclude isolates from Québec, and this must be considered when interpreting the data.

Seroprevalence for pneumococcal isolates recovered from blood and CSF for the past five years is presented in Table 6. With the exception of type 8, these same serotypes have consistently been among the top 12 for the past 5 years with only slight changes in ranking. The reason for an apparent increase in the prevalence of type 3 over the past 3 years is unclear.

Table 6. Comparative Ranking of the Most Common Serotypes April 1, 1999 - March 31, 2004

Serotype	2003-04	2002-03	2001-02	2000-01	1999-2000
Type 14	1	1	1	1	1
Type 4	2	2	2	2	5
Type 9V	3-4	5	3	5	4
Type 3	3-4	8	6	11/12	11
Type 6B	5	4	5	3	2
Type 18C	6	7	4	6	7
Type 23F	7	6	11	10	6
Type 19F	8	3	7	4	3
Type 8	9	13	10	11/12	16
Type 22F	10	9	8	9	8
Total cases	823	828	703	670	772

All serotypes listed in table 6 are included in the currently available 23-valent vaccine. Overall, vaccine coverage can be expected for 91% of the total cases represented in the 2003/04 collection, and 89% if the expected cross-protection for serotype 6A is excluded. A comparison of vaccine coverage for the past five years is presented in Table 7.

Table 7. Vaccine coverage (23-valent) with and without type 6A (cross-protection expected)

	2003-04	2002-03	2001-02	2000-01	1999-2000
Percent coverage including serotype 6A	91	93	93	92	93
Percent coverage without serotype 6A	87	89	90	89	90

As in previous years, Alberta is disproportionately represented in this collection, presumably because of proximity and community awareness of national and provincial surveillance programs. Forty-four percent (358 of 823 isolates) of the 2003/04 sample was from Alberta. Because of this obvious bias, Table 8 presents Alberta data separately from the rest of Canada (TROC).

With the exception of type 9N, the top 13 serotypes are the same for both Alberta and TROC. Type 14 continues to be the most common serotype across Canada. Over the past year, type 8 was more prevalent in Alberta than in other provinces accounting for 6.4% versus 3.0% of the collections, while type 9V was more commonly submitted from TROC (9.2% versus 4.7%). The increase in type 9N in Alberta over the past year is notable. We reported 12 isolates (3.4% of the Alberta collection) belonging to that serotype compared with only a single isolate from 2002/03.

Of interest is the increase in the number of nontypable isolates received during 2003-04. We were unable to type 11 strains (2.4%), all of which were submitted from the same province over a period of nine months (May/03-Jan/04). Consultation with the submitting laboratory indicated that there was no epidemiological association between these 11 cases, and preliminary fingerprinting (PFGE) suggests that the strains are unrelated.

Table 8. Serotype Distribution in Alberta compared with the rest of Canada (TROC) for 2003/04 Rank and Percent of the total for 2003/04 (comparable data for 2002/03)

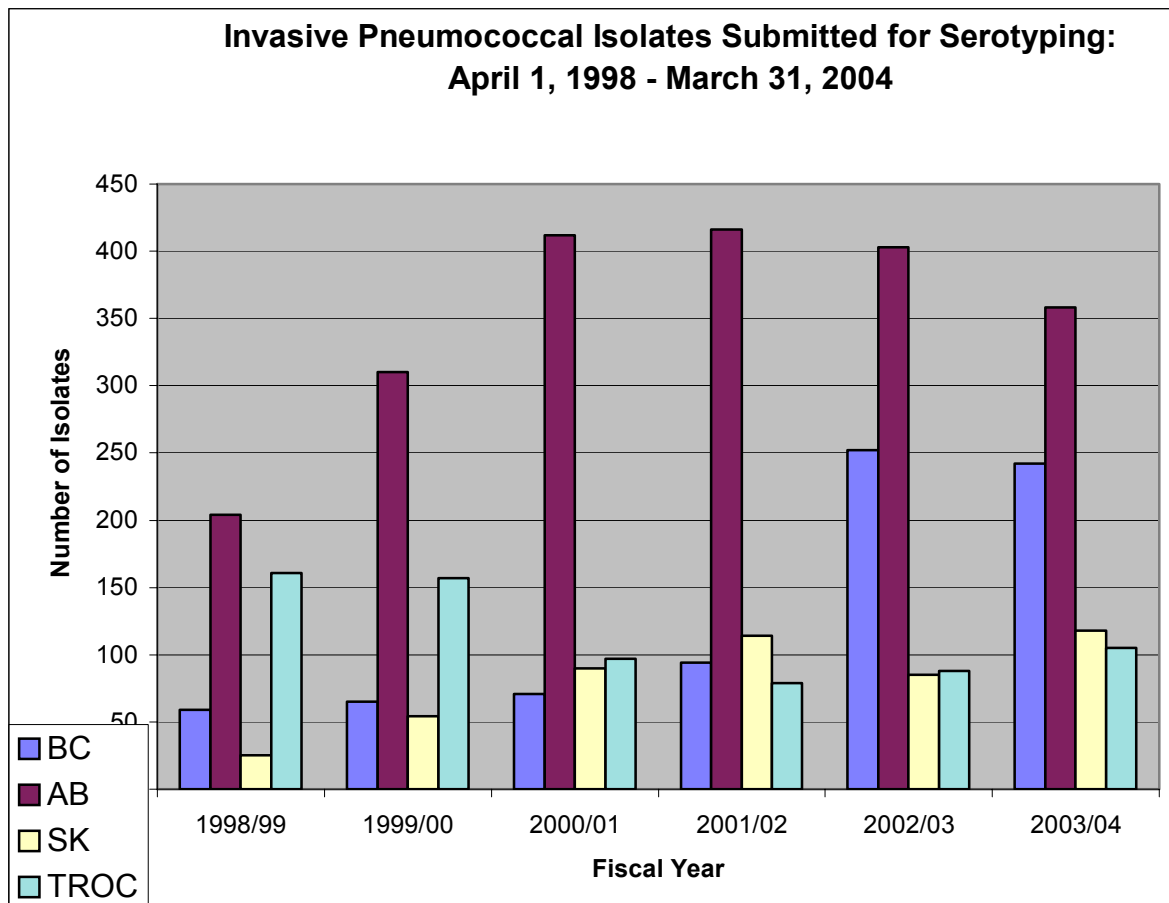
Serotype	Alberta		TROC	
	Rank	Percent of Total	Rank	Percent of Total
Type 14	1 (1)	12.6 (15.9)	1 (1)	17.0 (20.0)
Type 4	2 (2)	9.2 (10.4)	3 (2)	8.0 (8.2)
Type 6B	3 (3)	8.1 (7.0)	5 (6)	5.8 (6.8)
Type 3	4 (6)	6.4 (6.2)	4 (8)	7.3 (4.9)
Type 8	5 (10-12)	6.4 (4.2)	11 (14)	3.0 (2.1)
Type 18C	6 (7)	5.9 (5.5)	8 (7)	5.2 (5.9)
Type 9V	7-8 (8)	4.7 (5.2)	2 (3)	9.2 (7.5)
Type 23F	7-8 (10-12)	4.7 (4.2)	6-7 (4-5)	5.6 (7.3)
Type 19F	9 (4)	4.5 (6.7)	6-7 (4-5)	5.6 (7.3)
Type 7F	10 (13)	4.2 (4.0)	14 (12)	2.4 (2.6)
Type 1	11 (10-12)	3.6 (4.2)	12-13 (13)	2.6 (2.2)
Type 9N	12 (*)	3.4 (*)	15 (17)	1.7 (1.1)
Type 22F	13 (5)	3.0 (6.5)	9 (9)	4.7 (4.0)
Other Types		23.3 (19.8)		19.5 (19.2)
Nontypable		0(0)		2.4 (0.9)
Total # cases		358 (403)		465 (425)

* 1 isolate received

The majority of the pneumococcal isolates that are submitted to the NCS for routine serotyping are from Western Canada. A comparison of the number of isolates submitted from the 3 western most provinces compared with those submitted from the rest of Canada (TROC), excluding Quebec, is presented in Figure 4. Based on the limited number of isolates received from provinces east of Saskatchewan, it appears that only selected pneumococcal isolates from those regions are submitted for serotyping.

The increase observed for Alberta after 1998 was due to the implementation of a Provincial surveillance program in the fall of that year, to monitor invasive pneumococcal disease. In August, 2002 Alberta added Pevnar™ to the childhood vaccination program for children under 2 years of age. The reduction in the number of pneumococcal isolates received between April 1, 2003 and March 31, 2004 was seen specifically in the under 5 age group (table 9) and it is tempting to attribute this to the implementation of this important public health intervention.

Figure 4. Pneumococcal Isolates Submitted to the NCS. (Excludes Quebec)



The serotypes that cause invasive disease in young children are known to be different from those causing disease in older patients. The data for April 1, 2003 – March 31, 2004 are presented in tables 9 and 10 sorted according to patient age. Comparative data for the previous year are also provided.

Table 9. Serotype Distribution for Children (≤ 16 years) for April 1, 2003 - March 31, 2004
(Comparative data for April 1, 2002 - March 31, 2003)

Serotype	≤ 5 years	6 - 16 years	Total ≤ 16 years	
	# Cases	# Cases	# Cases	Rank
Type 14*	54 (76)	2(4)	56(80)	1(1)
Type 6B*	24(29)	3(1)	27(30)	2(3)
Type 19F*	22(30)	0(1)	22(31)	3(2)
Type 23F*	13(15)	2(1)	15(16)	4-6(6)
Type 18C*	10(20)	5(6)	15(26)	4-6(4)
Type 9V*	13(6)	2(9)	15(15)	4-6(7)
Type 6A	10(13)	0(0)	10(13)	7(8)
Type 1	3(4)	5 (4)	8(8)	8(9)
Type 4*	6(16)	1(2)	7(18)	9(5)
Type 3	4(0)	2(3)	6(3)	10(15)
Type 19A	5(6)	0(1)	5(7)	11-12(10)
Type 22F	4(5)	1(1)	5(6)	11-12(11)
Other Types	22(24)	8(9)	30(33)	
Total No. Cases	190(244)	31(42)	221(286)	

* Serotypes included in the heptavalent conjugate vaccines

Seventy-five percent of the isolates submitted between April 1, 2003 and March 31, 2004 from children ≤ 5 years of age (142 of 190 isolates), and 79% of those from the same age group submitted between April 1, 2002 and March 31, 2003 (192 of 244 isolates) belong to the seven serotypes which are included in the heptavalent conjugate vaccines. If the expected cross-protection against type 6A is included, coverage increases to 80% for 2003/04 and 84% for 2002/03.

Serotype 14 continues to be the most prevalent serotype in both adults and children. The presence of serotype 3 in the top ten serotypes recovered from children over the past year may be of concern. Type 3 is typically associated with adult disease and is not currently included in conjugate vaccine formulations. Between April 1, 2003 and March 31, 2004 we received type 3 isolates from four children of less than five years of age; one from CSF, age 3 months and three from blood cultures, ages 3 weeks to 4 years. While this is a relatively small number of cases, it compares with only a single type 3 pediatric case in children ≤ 5 years over the preceding two years (April 1, 2001 – March 31, 2003). It will be important to monitor this shift, and potentially other changes in serotypes causing disease in young children as a possible outcome to the implementation of new conjugate vaccines in this age group.

Table 10. Serotype Distribution for Adults (≥ 17 years) for April 1, 2003 – March 31, 2004
(Comparative data for April 1, 2002 - March 31, 2003)

Serotype	17-64 years	≥ 65 years	Total ≥ 17 years	
	# Cases	# Cases	# Cases	Rank
Type 14*	42(40)	26(29)	68(69)	1(1)
Type 4*	53(46)	10(13)	63(59)	2(2)
Type 3*	28(19)	26(24)	54(43)	3(3)
Type 9V*	29(23)	16(15)	45(38)	4(4)
Type 8*	29(20)	6(5)	35(25)	5(9)
Type 18C*	19(14)	11(7)	30(21)	6(11)
Type 6B*	16(12)	13(15)	29(27)	7(7-8)
Type 22F*	13(21)	15(16)	28(37)	8-9(5)
Type 23F*	12(16)	16(16)	28(32)	8-9(6)
Type 7F*	18(19)	4(5)	22(24)	10(10)
Type 9N*	12(1)	8(2)	20(3)	11(22)
Type 19F*	11(16)	8(11)	20^(27)	12 (7-8)
Type 6A	9(10)	9(10)	18(20)	13(12)
Type 1*	16(17)	1(2)	17(19)	14-15(13)
Type 19A	11(6)	8(1)	17(7)	14-15(17)
Type 11A*	7(6)	6(6)	13(12)	16(15)
Other Types	62(57)	31(22)	95(79)	
Total No. Cases	387(343)	214(199)	602^(542)	

* Serotypes included in the 23-valent vaccine

^ Includes one adult case for which age was not available

Serotypes 7F, 8, 9N and 11A were recovered from the adult population, but rarely from young (≤ 5 yrs) children. The 23-valent vaccine (Pneumovax™) would provide coverage for 89% (536 of 602) of the invasive adult isolates submitted between April 1, 2003 and March 31, 2004 and 92% (498 of 542), of those submitted from April 1, 2002 – March 31, 2003 assuming cross-protection for types 6A and 6B. Similarly, the 23-valent vaccine, which is recommended for use in the ≥ 65 age group, would provide coverage for 89% (191 of 214) of the isolates recovered from those cases.

Fourty isolates from cerebrospinal fluid were submitted. These belonged to 17 different serotypes; one strain was nontypable. Eleven of the 40 cases had an accompanying blood isolate; the serotype of these isolates always matched the serotype of the CSF isolate. Cases were distributed over all age ranges; 13 (33%) were from patients ≤ 16 years of age including 9 from children ≤ 2 years. Of 27 isolates from the ≥ 17 year old age group, only 6 patients were ≥ 65 , the largest target group for the 23-valent conjugate vaccines. Table 11 compares the serotype with the age range of the patients from whom the pneumococci were isolated from CSF.

Table 11. Comparison of serotype & age range for pneumococci from CSF for Apr 1/03 - Mar 31/04.

Serotype	≤ 2 years	3-5 years	6-16 years	17-64 years	≥ 65 years	Total
Type 14 ^Δ	1			3	2	6
Type 3 ^Δ	1			3		4
Type 6B ^Δ	2			1	1	4
Type 18C ^Δ			1	3		4
Type 6A		1		2		3
Type 7F ^Δ	1			1	1	3
Type 4 ^Δ				2		2
Type 9V ^Δ				1	1	2
Type 15C				2		2
Type 19F ^Δ	1	1				2
Type 23F ^Δ					1	1
Type 15A			1			1
Type 19A ^Δ				1		1
Type 8 ^Δ	1					1
Type 9N ^Δ				1		1
Type 12F ^Δ	1					1
Type 35F				1		1
Nontypable	1					1
Total	9	2	2	21	6	40

^Δ Serotypes included in the 23-valent vaccine (Pneumovax™)

Streptococcus pneumoniae and Antibiotic Resistance

As of April 1, 2000 susceptibility testing of chloramphenicol, clindamycin, erythromycin, ofloxacin, trimethoprim-sulfamethoxazole and vancomycin was implemented for all invasive pneumococci submitted to the NCS for serotyping (excluding Quebec). In April, 2002, ofloxacin was replaced by levofloxacin as the representative quinolone in our testing panel. The minimum inhibitory concentration was determined by the National Committee for Clinical Laboratory Standards (NCCLS) recommended broth microdilution method.

Because isolates from Alberta account for almost half of this collection, antibiotic resistance data have been analyzed separately in Tables 12, 13 and 16. The proportion of intermediate and full resistance to seven antibiotics for Alberta compared with the rest of Canada (TROC) is presented in Table 12. These data are analyzed separately for children (≤ 16 yrs) and adults (≥ 17 yrs) in tables 13 and 16. As expected, all isolates were susceptible to vancomycin.

Table 12. Proportion (%) of Antibiotic Resistance by Region for Pneumococci;
Analysis for All Ages: from April 1, 2003 - March 31, 2004
 (Comparative data for April 1/02 - March 31/03)

Antibiotic	Interpretive Category	Alberta # of isolates = 358(403)	TROC # of isolates = 465(425)	Total for Canada # isolates = 823(828)
Penicillin	Intermediate	6.4(6.5)	7.7(6.6)	7.2(6.5)
	Resistant	1.4(2.2)	4.7(3.3)	3.3(2.8)
	Total	7.8(8.7)	12.5(9.9)	10.5(9.3)
Ceftriaxone	Intermediate	0(0.3)	0.4(0.5)	0.2(0.4)
	Resistant	0(0)	0(0)	0(0)
	Total	0(0.3)	0.4(0.5)	0.2(0.4)
Chloramphenicol	Intermediate	0(0)	0(0)	0(0)
	Resistant	0.3(1.5)	1.3(2.4)	0.9(1.9)
	Total	0.3(1.5)	1.3(2.4)	0.9(1.9)
Clindamycin	Intermediate	0.3(0)	0(0)	0.1(0)
	Resistant	2.8(3.0)	2.2(2.8)	2.4(2.9)
	Total	3.1(3.0)	2.2(2.8)	2.6(2.9)
Erythromycin	Intermediate	0(0.3)	0(0)	0(0.1)
	Resistant	8.9(7.9)	9.5(9.6)	9.2(8.8)
	Total	8.9(8.2)	9.5(9.6)	9.2(8.9)
Levofloxacin	Intermediate	0(0)	0(0)	0(0)
	Resistant	0.6(0)	0(0.7)	0.2(0.4)
	Total	0.6(0)	0(0.7)	0.2(0.4)
Trimethoprim-Sulfamethoxazole	Intermediate	9.8(10.9)	5.8(7.3)	7.5(9.1)
	Resistant	6.7(11.4)	13.8(10.4)	10.7(10.9)
	Total	16.5(22.3)	19.6(17.6)	18.2(19.9)

Table 13. Proportion (%) of Antibiotic Resistance by Region for Pneumococci;
For children (≤16 yrs); from April 1, 2003 – March 31, 2004
 (comparative data for April 1/02 - March 31/03)

Antibiotic	Interpretive Category	Alberta # of isolates = 78(125)	TROC # of isolates = 143(161)	Total for Canada # isolates = 221(286)
Penicillin	Intermediate Resistant	7.7(9.6) 0(2.4)	7.0(8.1) 7.7(5.0)	7.2(8.7) 5.0(3.9)
	Total	7.7(12.0)	14.7(13.0)	12.2(12.6)
Ceftriaxone	Intermediate Resistant	0(0.8) 0(0)	1.4(0.6) 0(0)	0.9(0.7) 0(0)
	Total	0(0.8)	1.4(0.6)	0.9(0.7)
Chloramphenicol	Intermediate Resistant	0(0) 0(3.2)	0(0) 2.1(3.1)	0(0) 1.4(3.2)
	Total	0(3.2)	2.1(3.1)	1.4(3.2)
Clindamycin	Intermediate Resistant	0(0) 1.3(4.0)	0(0) 4.9(5.0)	0(0) 3.6(4.6)
	Total	1.3(4.0)	4.9(5.0)	3.6(4.6)
Erythromycin	Intermediate Resistant	0(0) 7.7(11.2)	0(0) 13.3(11.2)	0(0) 11.3(11.2)
	Total	7.7(11.2)	13.3(11.2)	11.3(11.2)
Levofloxacin	Intermediate Resistant	0(0) 0(0)	0(0) 0(0)	0(0) 0(0)
	Total	0(0)	0(0)	0(0)
Trimethoprim-Sulfamethoxazole	Intermediate Resistant	12.8(12.8) 7.7(13.6)	7.7(6.2) 18.2(13.0)	9.5(9.1) 14.5(13.3)
	Total	20.5(26.4)	25.9(19.3)	24.0(22.4)

In January, 2002, the NCCLS modified the interpretive standard for pneumococci when testing ceftriaxone, cefotaxime and cefepime (Document M100-S12). The MIC breakpoints for these drugs for pneumococci isolated from patients with meningitis are now interpreted differently from pneumococci isolated from non-meningitis cases. The new interpretation for all three antibiotics is provided in Table 14.

Table 14. Jan, 2002 NCCLS ceftriaxone, cefotaxime & cefepime interpretive standards for *S. pneumoniae*

	Susceptible MIC breakpoint	Intermediate MIC breakpoint	Resistant MIC breakpoint
Meningitis	≤0.5 µg/ml	1.0 µg/ml	≥2.0 µg/ml
Nonmeningitis	≤1.0 µg/ml	2.0 µg/ml	≥4.0 µg/ml

Because the interpretation of the ceftriaxone MIC is dependent upon whether or not the patient has meningitis, a breakdown of that MIC interpretation by specimen source is provided in Tables 14 and 16.

Table 15. **Ceftriaxone interpretation** for pneumococci from **children (≤16 yrs)** (April 1/03 - March 31/04) by specimen source according to NCCLS Document M100-S12, January, 2002

Specimen Source	ALBERTA			TROC			TOTAL		
	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant
Blood/nonmeningitis	74	0	0	134	2	0	208	2	0
CSF/meningitis	4	0	0	9	0	0	13	0	0
Total	78	0	0	143	2	0	221	2	0

Overall, there were only small changes in rates of antibiotic resistance when data for 03/04 are compared with the previous year (02/03). For children from Alberta, however, there appears to be a substantial reduction in the number of isolates with reduced susceptibility to both penicillin and erythromycin (7.7% versus 12% and 7.7% versus 11.2% respectively). There is also an encouraging reduction in resistance to trimethoprim/sulfamethoxazole for this age group.

There were only slight changes in antibiotic resistance patterns for adults over the past year (Table 16). Unlike the younger age group, there was an increase in reduced susceptibility to penicillin. This change was very small in Alberta (7.9% versus 7.2%), but for isolates submitted from the rest of Canada, the rate increased from 8% to 11.5%. There is also a continuing increase in clindamycin resistance observed in Alberta. This has climbed to 3.6% from a low of 0.4% in 01/02. As well, erythromycin resistance increased to 9.3%, even though the rate appears to have dropped for isolates submitted from the rest of Canada.

Table 16. Proportion (%) of Antibiotic Resistance by Region for Pneumococci;
For adults (≥17 yrs); from April 1, 2003 – March 31, 2004
 (comparative data for April 1/02 - March 31/03)

Antibiotic	Interpretive Category	Alberta # of isolates = 280(278)	TROC # of isolates = 322(264)	Total for Canada # isolates = 602(542)
Penicillin	Intermediate	6.1(5.0)	8.1(5.7)	7.1(5.4)
	Resistant	1.8(2.2)	3.4(2.3)	2.7(2.2)
	Total	7.9(7.2)	11.5(8.0)	9.8(7.6)
Ceftriaxone	Intermediate	0(0)	0(0.4)	0(0.2)
	Resistant	0(0)	0(0.6)	0(0)
	Total	0(0)	0(0.4)	0(0.2)
Chloramphenicol	Intermediate	0(0)	0(0)	0(0)
	Resistant	0.4(0.7)	0.9(1.9)	0.7(1.3)
	Total	0.4(0.7)	0.9(1.9)	0.7(1.3)
Clindamycin	Intermediate	0.4(0)	0(0)	0.2(0)
	Resistant	3.2(2.5)	0.9(1.5)	2.0(2.0)
	Total	3.6(2.5)	0.9(1.5)	2.2(2.0)
Erythromycin	Intermediate	0(0.4)	0(0)	0(0.0)
	Resistant	9.3(6.5)	7.8(8.7)	8.5(7.6)
	Total	9.3(6.8)	7.8(8.7)	8.5(7.8)
Levofloxacin	Intermediate	0(0)	0(0)	0(0)
	Resistant	0.7(0)	0(1.1)	0.3(0.6)
	Total	0.7(0)	0(1.1)	0.3(0.6)
Trimethoprim-Sulfamethoxazole	Intermediate	8.9(10.1)	5.0(8.0)	6.8(9.0)
	Resistant	6.1(10.4)	11.8(8.7)	9.1(9.6)
	Total	15.0(20.5)	16.8(16.7)	15.9(18.6)

Table 17. **Ceftriaxone interpretation** for pneumococci from **adults (≥17 yrs)** (April 1/03 - March 31/04)
 by by specimen source according to NCCLS Document M100-S12, January, 2002

Specimen Source	ALBERTA			TROC			TOTAL		
	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant	# Isolates	Inter-mediate	Resis-tant
Blood/nonmeningitis	263	0	0	312	0	0	575	0	0
CSF/meningitis	17	0	0	10	0	0	27	0	0
Total	280	0	0	322	0	0	602	0	0

General observations of antibiotic resistance for all ages

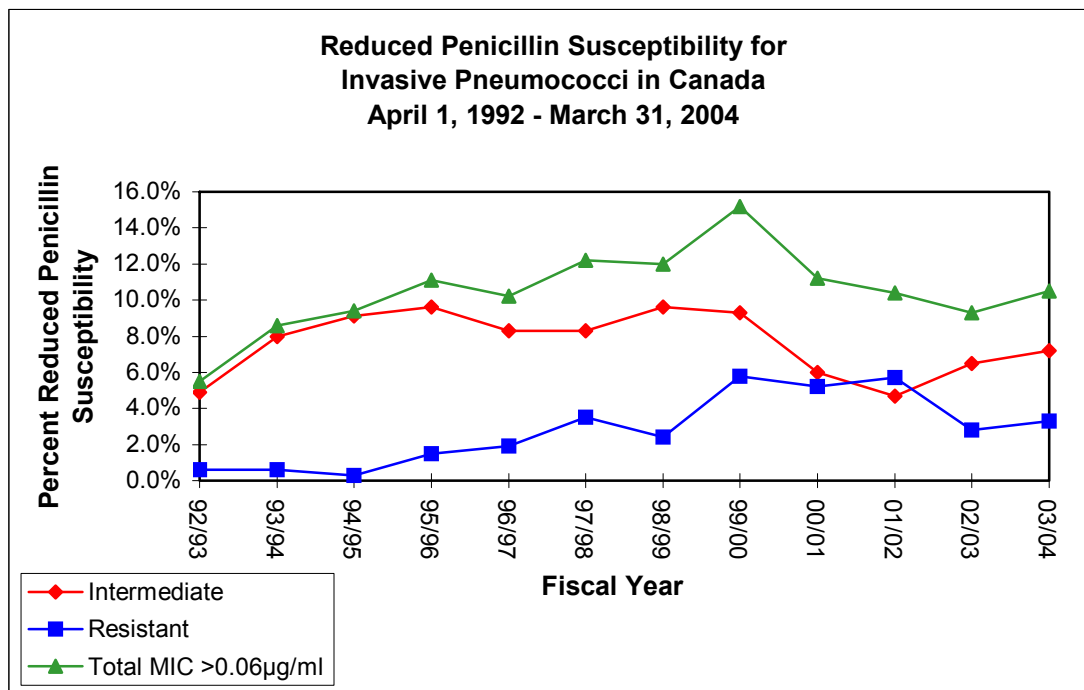
Reduced susceptibility to penicillin was detected in 86 isolates belonging to 10 different serotypes. Ninety-nine percent of these (85 of 86) are covered by the 23-valent vaccine if one assumes cross-protection for serotype 6A. Thirty-one percent (27 of 86) of these strains are fully resistant to penicillin (MIC ≥ 2.0 $\mu\text{g/ml}$). Reduced susceptibility to penicillin may be expected for type 19A. Of 17 type 19A isolates tested in 03/04, 11 (65%) showed intermediate resistance (MIC 0.12-1.0 $\mu\text{g/ml}$) and one was fully resistant. An increased likelihood of penicillin resistance is also associated with type 9V. Sixty-seven percent (40 of 60) of the type 9V isolates tested showed some level of resistance to penicillin; 27 were intermediate and 13 were resistant.

As observed in previous years, resistance to erythromycin and to trimethoprim-sulfamethoxazole frequently occurred in the absence of reduced susceptibility to penicillin. Fifty-nine percent (45 of 76) erythromycin-resistant pneumococci and 53% (79 of 150) of the trimethoprim-sulfamethoxazole-resistant pneumococci were susceptible to penicillin. This may be clinically relevant if antibiotic resistance observed for our invasive isolates can be extrapolated to pneumococci causing non-invasive disease. Both drugs are frequently used to treat respiratory infections.

We have defined multiple resistance as intermediate or full resistance to three different classes of antibiotics. Thirty-two of 823 isolates (3.9%) were multiply resistant; 29 of these had reduced susceptibility to penicillin. Multiple resistance was demonstrated in serotypes 6B (6 isolates), 14 (6 isolates), 23F (6 isolates), 19A (4 isolates), 6A (3 isolates), 9V (3 isolate), 19F (3 isolate), and 3 (1 isolate).

The steadily decreasing rates of penicillin resistance that we have enjoyed since 2000 were halted last year when the overall rate increased from 9.3% in 02/03 to 10.5% in 03/04 (Figure 5). This may simply represent sampling bias specifically for isolates that were submitted from the rest of Canada rather than signaling a true increase, since the Alberta rates continued to decline.

Figure 5.



c. Outbreak Investigation

Tracking outbreak and/or clusters of streptococcal infection is sometimes difficult since a description of the event is not always submitted. When non-invasive isolates are received in this laboratory, follow up is initiated to determine the reason for the test request. It is often only after this type of contact with the submitting agency that we are able to identify the group of specimens as part of an outbreak investigation. We encourage laboratory directors to reinforce the importance of submitting outbreak documentation to the NCS, and recruiting the assistance of their local outbreak investigation teams in this regard.

During the past year the NCS was asked to provide laboratory testing for 8 epidemiological investigations conducted in 5 provinces. The investigations conducted during 2003/04 are listed in Table 18.

Table 18. Summary of Epidemiologic Investigations April 1, 2003 - March 31, 2004

Investigation Number	Province Requesting Investigation	Test Request	No. of Samples	Causative Agent
03-5006	Ontario	GAS serotyping investigation of nursing home outbreak	4	M4 T4 AOF4 OF + (case & one contact) M1 T1 OF – (2 contacts)
03-5007	Quebec	GAS serotyping investigation of 2 invasive cases	4	M nontypable T11/28 AOF 28 OF + (2 cases) M5 T5 OF – (one contact) M12 T nontypable OF- (one contact)
03-5008	Ontario	GAS serotyping investigation – no details provided	5	M22 T12 AOF22 OF + (2 cases & 2 contacts) M6 T6 OF – (one contact)
03-5009	Ontario	GAS serotyping investigation of nursing home contacts of necrotizing fasciitis (1 case)	6	M nontypable T5/27/44 AOF82 OF + (case & 2 contacts) 3 unrelated M types from 3 contacts
03-274	Alberta	GAS serotyping -cluster of GAS non-invasive infections related to a single work site	3	M92 Timp19 AOF92 OF + (3 isolates)
03-5010	British Columbia	Investigation (PFGE) of cluster of 4 nontypable invasive S. pneumoniae cases	4	PFGE patterns unrelated – no epidemiological link
04-5000	Nova Scotia	GAS serotyping investigation of cluster of invasive disease	5	M1 T1 OF – (2 cases) M nontypable T28 AOF28 OF + (1 case) M3 T3/13 OF – (one case) M12 T12 OF – (one case)
04-60	Alberta	GAS serotyping investigation of nursing home outbreak	2	M77 T13/28 AOF77 OF + (2 isolates)
04-5001	Alberta	GAS serotyping investigation of health care workers and case	4	M75 T25/Imp19 AOF75 OF + (4 isolates)

d. Research

Table 18 lists completed and/or on-going research projects in which the National Centre for Streptococcus participated during 2003 - 2004.

Streptococcus pneumoniae

Table 18. Summary of Research Projects April 1, 2003 - March 31, 2004

Researcher/Agency	Study Description	Services Required
Pan American Health Organization with funding from the Canadian International Development Agency	SIREVA Project - determination of pneumococcal seroprevalence and antibiotic resistance rates in Latin American children <5 yrs of age	SIREVA Network now includes 23 countries in Central and South America. NCS continues to provide leadership and technical resources for the Quality Assurance program
Immunization Monitoring Program, Active (IMPACT) Dr. David Scheifele	Surveillance of invasive pneumococci recovered from Canadian children ≤16 yrs of age	Pneumococcal serotyping and antibiotic susceptibility testing
Dr. Jim Kellner, Alberta Children's Hospital, Calgary, Alberta	Surveillance of invasive pneumococcal disease within the Calgary Regional Health Authority	Pneumococcal serotyping
Dr. Tom Marrie University of Alberta Hospital Edmonton, Alberta	Investigation of community acquired pneumonia and invasive disease in the Capital Health Region	Pneumococcal serotyping and antibiotic susceptibility testing
Dr Fred Aoki, Health Sciences Centre, Winnipeg, Manitoba	Morbidity, Mortality and Health Care Costs of Invasive Pneumococcal Disease in Manitobans	Pneumococcal serotyping
Dr. Alan Parkinson, Arctic Investigations Program, Anchorage, Alaska	International Circumpolar Surveillance of Invasive Pneumococcal Disease	Pneumococcal serotyping and antibiotic susceptibility testing
Dr. Barbara Jantusch Children's National Medical Centre, Washington DC	Investigation of Invasive Pneumococcal Disease in Children	Pneumococcal serotyping

Group A Streptococci (*Streptococcus pyogenes*)

Researcher/Agency	Study Description	Services Required
Dr. Alan Parkinson, Arctic Investigations Program, Anchorage, Alaska	International Circumpolar Surveillance of Invasive GAS Disease	GAS serotyping and antibiotic susceptibility testing
Mark Reddish ID Biomedical/ID Vaccine Corp. Bothell, Washington	StreptAvax™ GAS Vaccine trials	Phase 1 Safety trials - GAS serotyping Contribution to design and participation in Phase 2 Canadian trials planned

Group B Streptococcus (*Streptococcus agalactiae*)

Researcher/Agency	Study Description	Services Required
Dr. Alan Parkinson, Arctic Investigations Program, Anchorage, Alaska	International Circumpolar Surveillance of Invasive GBS Disease	GBS serotyping and antibiotic susceptibility testing
Belgin Dogan Food Science Dept. Cornell University New York, NY	Milk Quality Survey	Group B serotyping

Other Investigations

Researcher/Agency	Study Description	Services Required
Dr. Richard Facklam Centres for Disease Control, Atlanta, Georgia	Collaborative investigation of new <i>Aerococcus</i> species	Identification

e. Training

There were no formal training events held during 2003/04.

Quality Indicators Monitored

1. Turn Around Time

The average turn around times (TAT) for the past year are compared with those for 2002/03 in Table 20. Testing for isolates that are associated with designated outbreak investigations are given priority status and the TAT will be significantly reduced from the averages reported here.

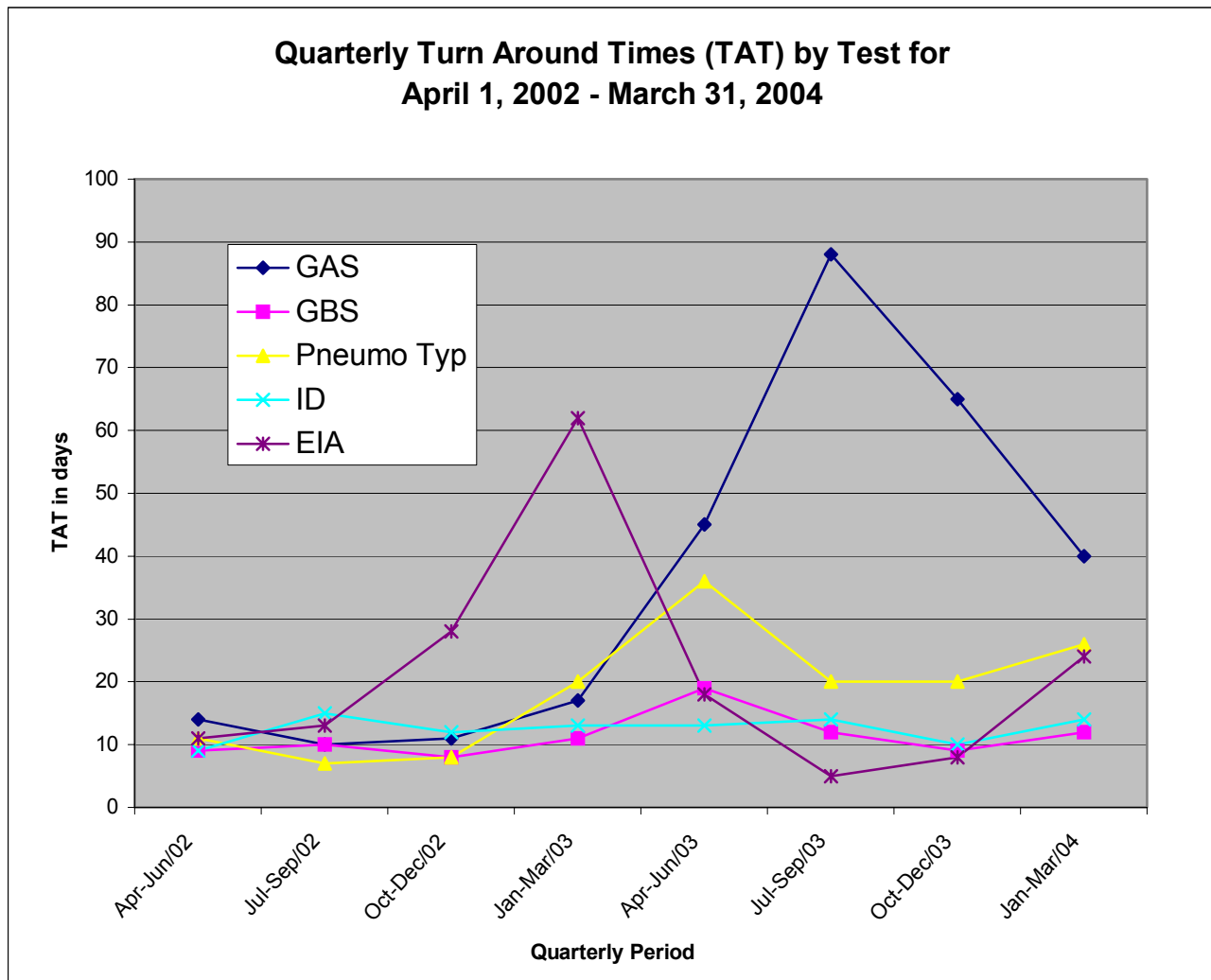
The increase in average TAT this year over last year is related to two issues: first, reduced staffing in early 2003 which resulted in a significant backlog of testing, and secondly, a shift toward submission of large batches of isolates, rather than more frequent submission of individual isolates. Managing these large specimen loads has resulted in an extended TAT especially for Group A streptococci and pneumococci. We understand the efficiencies that our customers gain through 'batching', and we ask for your patience with the extended TATs that result at our end from processing of large batches of specimens.

Group A *Streptococcus* serotyping was the test for which the most significant increase in TAT was observed. We are pleased that this TAT has gradually improved (Figure 6) and we anticipate that it will continue to do so over the coming months.

Table 20. Average Turn Around Time (TAT) for April 1, 2003 - March 31, 2004 compared to 2002/03

Test Request	Apr 1/03 - Mar 31/04 Avg. TAT in days	Apr 1/02 - Mar 31/03 Avg. TAT in days
Group A Serotyping	59	13
Group B Serotyping	13	10
<i>Streptococcus pneumoniae</i> Serotyping	26	12
Identification	13	13
Pneumococcal Serology	13	28

Figure 6.



2. Proficiency Testing Programs

Streptococcus pneumoniae Serotyping and Susceptibility testing - The NCS continues to participate in a collaborative Quality Control program involving the Laboratoire de Santé Publique du Québec and the Arctic Investigation Program laboratory in Anchorage, Alaska. This external quality assurance initiative supports the International Circumpolar Surveillance (ICS) program that now includes the northern regions of Canada, Alaska USA, Iceland, Greenland, Norway and Finland. We look forward to expansion of the ICS QC program to include the Statens Serum Institut in Copenhagen, Denmark in the coming year.

Over the past year three panels have been distributed. Correlation for serotyping data for all three labs was 100%. This is the fourth consecutive year that all centres have achieved this excellent agreement. The three laboratories achieved 94-100% correlation with MIC values within +/- one log₂ dilution for nine antibiotics that are routinely tested.

The NCS continues to serve as a resource for both education and Quality Assurance for the Sireva Project in Latin America. Consistent with the new model established in 1999, we work primarily with the three Quality Control Centres (Mexico, Colombia and Brazil), and continue to coordinate an external quality control program with semiannual distributions of pneumococci for serotyping and MIC testing.

Future Plans

As of March 31, 2004, the NCS has not yet reached agreement for additional Federal funding to proceed with some of our planned projects. As a result, these plans remain tentative. We look forward to enhancing our services and are hopeful that the necessary financial support that will enable us to do so will become available in the near future.

1. Implement *emm* sequencing for group A streptococci that prove to be M non-typable by serologic methods. The antisera used for this testing are not commercially available, and the in-house preparation, absorption and QC testing is very specialized and labor intensive. We anticipate that molecular characterization may replace traditional serological typing in the future.
2. Implement *sic* gene sequencing as a tool for characterization of M1 group A *Streptococcus* strains that are associated with outbreaks.
3. Increase our pneumococcal antibiotic susceptibility testing panel from 9 to 18 antibiotics. This would provide a broader scope of information on which to base national and provincial empiric therapy guidelines, and would also enable us to compare our resistance data with similar programs in the United States.
4. Initiate routine molecular investigation of antibiotic resistant pneumococcal isolates that are frequently encountered at the NCS. We hope to be able to determine which of the 26 currently recognized international antibiotic-resistant clones are circulating in the Canadian population.
5. Supplement the routine biochemical identification of atypical catalase-negative gram positive cocci with 16S rRNA sequencing. This additional tool would be provided only for isolates that are not easily identified by traditional biochemical testing.

Publications

1. Facklam, R.R., **M. Lovgren**, P.L. Shewmaker and **G.J. Tyrrell**. 2003. Phenotypic description and antimicrobial susceptibilities of *Aerococcus sanguicola* isolated from human clinical samples. *Journal of Clinical Microbiology*; 41:2587-2592
2. Allen, U.D., S. Thomas, J. Carapetis, S. Henry, S. Wasfy, **M. Lovgren**, S. Richardson and D.E. Low. 2003. Serotypes of respiratory tract isolates of *Streptococcus pneumoniae* from Jamaican Children. *International Journal of Infectious Disease*;7:29-35.
3. Smith, A., A. Li, O. Tolomeo, **G.J. Tyrrell**, F. Jamieson and D. Fisman. 2003, Mass antibiotic treatment for group A streptococcus outbreaks in two long term care facilities. *Emerging Infectious Disease*;9:1260-1265.
4. Vanderkooi, O.G., J.D. Kellner, A.W. Wade, T. Jadavji, J.P. Midgley, T. Louie and **G.J. Tyrrell**. 2003. *Canadian Journal of Infectious Disease*;14:339-343.
5. Burnham, C.A. and **G.J. Tyrrell**. 2003. Virulence Factors of Group B *Streptococcus*. *Reviews in Medical Microbiology*, 14:1-10.

Abstracts

1. **Tyrrell, G.J.**, B. Kress, **M. Lovgren** and K. Grimsrud. 2003. Invasive Group A Streptococcal Disease in Alberta, Canada 2000-2002. CACMID 2003, Montreal, Quebec, November 2-6, 2003.
2. Burnham, C.D., S.E. Shokoples and **G.J. Tyrrell**. 2003. Surface Associated Streptococcal Phosphoglycerate Kinase Binds Actin. CACMID 2003, Montreal, Quebec, November 2-6, 2003.
3. Burnham, C.A., S. Shokoples and **G.J. Tyrrell**. 2003. Surface Associated Streptococcal Phosphoglycerate Kinase Binds Actin. MacGregor Research Day. Department of Laboratory Medicine and Pathology, University of Alberta, September 25, 2003. (winner of MacGregor Prize for Graduate Students).
4. M. Bruce, T. Cottle, J. Butler, D. Parks, T. Tam, **M. Lovgren**, L. Jette, K. Kristinsson, G. Sigmundsdottir, F. Stenz, O. Lovoll, P. Nuorti, E. Herva, A. Parkinson. Use of the International Circumpolar Surveillance System for Population-based Surveillance of Invasive Pneumococcal Disease 1999-2001. Presented at the 12th *International Congress on Circumpolar Health*. Nuuk, Greenland 2003.

Invited Presentations

1. "Invasive Group A Streptococci in the USA, Canada and Alberta." Wit, Wisdom and Windows Educational Days. Education Event sponsored by the Department of Laboratory Medicine and Pathology, University of Alberta. January 21, 2003.
2. "Invasive Group A Streptococcal Disease". Medical Grand Rounds. University of Alberta Hospital, Edmonton, Alberta. January 10, 2003.

Staff

Director: Gregory Tyrrell PhD,FCCM,D(ABMM)
Phone: (780) 407 - 8949
Fax: (780) 407 - 7322
email: g.tyrrell@provlab.ab.ca

Technical Supervisor: Marguerite Lovgren MLT,ART
Phone: (780) 407 - 8977
Fax: (780) 407 - 8984
email: m.lovgren@provlab.ab.ca